

## ABSTRACT

The invention provides methods for efficient and rapid identification of cis-acting nucleic acid sequences that act in a cell-type or cell-state specific manner to stimulate or repress the expression of linked genes or other neighboring sequences. The invention also provides methods for evolving novel regulatory sequences by in vitro manipulation of naturally occurring or synthetic cis acting nucleic acid sequences followed by screening and counterscreening steps. Furthermore, the invention provides methods for determining the mechanism by which cell-type specific cis regulatory sequences confer cell-specific expression. Also provided are diagnostic methods based on the use of cell-specific cis regulatory sequences.

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